IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

ORIGINAL

In re application of:

ZAUDERER *et al.*

Appl. No. 09/987,456

Filed: November 14, 2001

For: ***In Vitro* Methods of Producing and Identifying Immunoglobulin Molecules in Eukaryotic Cells**

Confirmation No.: 6770

Art Unit: 1639

Examiner: Epperson, J.D.

Atty. Docket: 1821.0070004/EJH/T-M

Declaration Under 37 C.F.R. § 1.132

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Sir:

I, the undersigned, Dr. Walter J. Storkus, residing at 3303 Mount Royal Boulevard, Glenshaw, PA 15116, USA, declare and state as follows:

1. I was a member of the Scientific Advisory Board ("SAB") of Vaccinex, Inc., from 2001 until 2004.

2. A current *curriculum vitae* is appended hereto as Exhibit A1.

3. I received my Ph.D. degree in Microbiology and Immunology from Duke University in 1986, evaluating the importance of MHC class I molecule expression by tumor cells in their ability to be recognized and killed by natural killer (NK) cells. Since that time, I have been an NIH-funded investigator targeting the development of tumor vaccines and immunotherapies for patients with cancer. I am currently a tenured full professor in the

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ORIGINAL

Declaration Under 37 C.F.R. § 1.132

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Sir:

I, the undersigned, Dr. Maurice Zauderer, residing at 44 Woodland Road, Pittsford, New York 14534, declare and state as follows:

1. I am the co-founder of Vaccinex, Inc., and have held the positions of President and Chief Executive Officer since April 6, 2001. I am also a co-inventor of the captioned patent application.

2. A current *curriculum vitae* is appended hereto as Exhibit B1.

3. I received my Ph.D. degree in cell biology from the Massachusetts Institute of Technology in 1972. From 1971 to 1975, I conducted postdoctoral research at various research institutions including the Albert Einstein College of Medicine in New York, and the National Institute for Medical Research in London. I was an Assistant Professor in the

July 1, 2005

CURRICULUM VITAE

NAME: Walter J. Storkus, Ph.D.

BIRTH DATE: February 10, 1959

POB: Brockton, MA

HOME ADDRESS: 3303 Mount Royal Boulevard
Glenshaw, PA 15116
T#412-492-9745

CITIZENSHIP: U.S.A.

BUSINESS ADDRESS: Department of Surgery
University of Pittsburgh School of Medicine
1.32e Hillman Cancer Center-UPCI Research Pavilion
5117 Centre Avenue
Pittsburgh, PA 15213
T# 412-623-3240
FAX# 412-623-7709
E-Mail# storkuswj@msx.upmc.edu

EDUCATION AND TRAINING

UNDERGRADUATE:

1977-1981	Brandeis University Waltham, MA 02154	B.A.	Biochemistry Mathematics

GRADUATE:

1982-1986	Duke University Durham, NC 27710	Ph.D.	Microbiology/ Immunology

Thesis: "NK Regulation of B cell Development"
Advisor: J.R. Dawson, Ph.D.

POST-GRADUATE:

1986-1987	Department of Microbiology and Immunology, Duke University Med. Ctr. Durham, NC 27710.	NIH Postdoctoral Fellow (J.R. Dawson, Ph.D.)
1987-1991	Department of Microbiology and Immunology, Duke University Med. Ctr. Durham, NC 27710.	Research Associate (P. Cresswell, Ph.D./ J.R. Dawson, Ph.D.)

APPOINTMENTS AND POSITIONS

ACADEMIC:

1985-1991	Department of Microbiology and Immunology, Duke University, Durham, NC 27710	Teaching Assistant

L.E.K.

VACCINEX, INC.

MAb Partnership Strategy
Final Presentation

November 1, 2001

Auckland
Bangkok
Beijing
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London
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Melbourne
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San Francisco
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Singapore
Sydney

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The materials contained in this document are intended to supplement a discussion between Vaccinex and L.E.K. Consulting on November 1, 2001. These perspectives are confidential and will only be meaningful to those in attendance.

THE JOURNAL OF BIOLOGICAL CHEMISTRY
Vol. 274, No. 26, Issue of June 25, pp. 18218–18230, 1999
Printed in U.S.A.

A Large Non-immunized Human Fab Fragment Phage Library That Permits Rapid Isolation and Kinetic Analysis of High Affinity Antibodies*

(Received for publication, December 7, 1998, and in revised form, April 9, 1999)

Hans J. de Haard‡§, Nicole van Neer‡, Anneke Reurs¶, Simon E. Hufton‡, Rob C. Roovers¶, Paula Henderikx¶, Adriaan P. de Bruïne¶, Jan-Willem Arends¶, and Hennie R. Hoogenboom‡¶‖

From ‡Target Quest B.V. and the ¶Department of Pathology, Maastricht University and University Hospital Maastricht, P.O. Box 5800, 6202 AZ Maastricht, The Netherlands

We report the design, construction, and use of the first very large non-immunized phage antibody library in Fab format, which allows the rapid isolation and affinity analysis of antigen-specific human antibody fragments. Individually cloned heavy and light chain variable region libraries were combined in an efficient two-step cloning procedure, permitting the cloning of a total of 3.7×10^{10} independent Fab clones. The performance of the library was determined by the successful selection of on average 14 different Fabs against 6 antigens tested. These include tetanus toxoid, the hapten phenyl-oxazolone, the breast cancer-associated MUC1 antigen, and three highly related glycoprotein hormones: human chorionic gonadotropin, human luteinizing hormone, and human follicle-stimulating hormone. In the latter category, a panel of either homone-specific or cross-reactive antibodies were identified. The design of the library permits the monitoring of selections with polyclonal phage preparations and to carry out large scale screening of antibody off-rates with unpurified Fab fragments on BIAcore. Antibodies with off-rates in the order of 10^{-2} to 10^{-4} s^{-1} and affinities up to 2.7 nM were recovered. The kinetics of these phage antibodies are of the same order of magnitude as antibodies associated with a secondary immune response. This new phage antibody library is set to become a valuable source of antibodies to many different targets, and to play a vital role in target discovery and validation in the area of functional genomics.

Display on filamentous phage in combination with selection forms a powerful tool for the identification of peptide- or protein-based drugs (1, 2). Of these, antibodies are especially of interest, due to their capacity to recognize a variety of targets with high specificity and affinity. In particular, the use of partially or completely human antibodies, which elicit no or minimal immune response when administered to patients, is yielding an increasing list of FDA-approved protein-based drugs (3). Phage display technology enables the generation of large repertoires of human antibodies (4–7), while the biopanning procedure permits the selection of individual antibodies with a desired specificity.

Key to the success of the technology were two critical observations: (i) the expression of functional antibody fragments by secretion into the periplasm of *Escherichia coli* (8, 9), and (ii) the rapid access to variable region gene pools by the polymerase chain reaction (10–12). For the construction of antibody libraries, V-genes are amplified from B cell cDNA and heavy and light chain genes are randomly combined and cloned to encode a combinatorial library of single-chain Fv (scFv)[1] or Fab antibody fragments (4, 13–15). The natural primary (unselected) antibody repertoire within B cells contains a large array of antibodies that recognize a variety of antigens; this array can be cloned as a "naïve" repertoire of rearranged genes, by harvesting the V-genes from the IgM mRNA of B cells of unimmunized human donors, isolated from peripheral blood lymphocytes (4), from bone marrow or tonsils (7), or from similar animal sources (16). This procedure provides access to antibodies that have not yet encountered antigen, although the frequency of those genuine "germline" antibodies will depend heavily on the source of B cells (17). A single naïve library, if sufficiently large and diverse, can indeed be used to generate antibodies to a large panel of antigens, including self, non-immunogenic and relatively toxic antigens (4, 6). In a different approach, antibodies may be built artificially, by *in vitro* assembly of V-gene segments and D/J segments, yielding "synthetic" antibodies (5). A major drawback of these procedures is that from the initial naïve and synthetic libraries, only moderate affinity antibodies were isolated (4, 18). Over the last few years, more efficient techniques have been developed to build larger libraries of antibody fragments, using sophisticated *in vivo* recombination methods (6) or brute force cloning procedures (7, 19). Such large libraries have yielded a greater number of human antibodies per antigen tested, with on average much higher affinity (up to subnanomolar). However, technical restrictions on the size of libraries that may be obtained or handled in selection, the loss of library diversity upon library amplification, and the relatively long downstream analysis path of the selected antibodies, *i.e.* large scale affinity analysis, have limited the spread of these libraries as generic tools in antibody generation.

We describe here the generation of a very large antibody library based on the display of Fab fragments on phage. The choice for the Fab format was based on the notion that the monomeric appearance of the Fab should permit the rapid screening of large numbers of clones on kinetics of binding

* This work was supported by European Community Biotechnology Program 5.1 Grant BIO4CT950252 (to P. H.). The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "*advertisement*" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

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‖ To whom correspondence and reprint requests should be addressed. Tel.: 31-433874630; Fax: 31-433874609; E-mail: hho@lpat.azm.nl.

[1] The abbreviations used are: scFv, single-chain Fv fragment; PCR, polymerase chain reaction; PBL, peripheral blood lymphocyte; BSA, bovine serum albumin; PBS, phosphate-buffered saline; ELISA, enzyme-linked immunosorbent assay; RU, resonance units; hCG, human chorionic gonadotropin; hLH, human luteinizing hormone; hFSH, human follicle-stimulating hormone; CTP, carboxyl-terminal peptide.

Exhibit **B1**
Appl. No. 09/987,456

Curriculum Vitae **August 4, 2004**

Maurice Zauderer, Ph.D.

Education

Yeshiva University; NY, New York	B.S.	1966	Physics
Massachusetts Institute of Technology; Cambridge, Massachusetts	Ph.D.	1972	Cell Biology

Professional Positions:

1971-1975 Postdoctoral Fellow of the Helen Hay Whitney Foundation.
1972-1973 Postdoctoral Research with Dr. Matthew D. Scharff, Albert Einstein College of Medicine, NY.
1974-1975 Postdoctoral Research with Dr. Brigitte A. Askonas, National Institute for Medical Research, Mill Hill, London.
1975-1976 Visiting Scientist Laboratory of Cell Biology, Rome, Italy
1976-1983 Assistant Professor, Department of Biological Sciences, Columbia, University, NY, NY.
1984-2000 Associate Professor, Cancer Center and Department of Microbiology and Immunology, University of Rochester, Rochester, NY.
1984-1985 Visiting Scientist, Laboratory of Dr. Tak Mak, Ontario Cancer Institute, Toronto, Canada.
1990- 1997 Associate Professor, Strong Children's Research Center and Department of Pediatrics, University of Rochester, Rochester, New York.
1993-1994 Visiting Scientist, Laboratory of Dr. Alfred Singer, Experimental Immunology Branch, NCI, NIH, Bethesda, MD.
1997-2001 President and General Partner of Vaccinex, LP
2001- President & CEO, Vaccinex, Inc., Rochester, N.Y.

Other Professional Activities:

1984 National Science Foundation, Cellular Physiology Study Section.
1987-1989 Associate Editor, Journal of Immunology.
1990 Allergy and Immunology Study Section, Division of Research Grants, N.I.H.
1990 National Cancer Institute Special Review Committee

Pharmaceuticals for Rare Diseases

OPi and Vaccinex announce antibody collaboration

Lyon, France and Rochester, USA, june 30, 2004. OPi and Vaccinex announced today a strategic collaboration to discover and develop novel monoclonal antibodies for the treatment of certain rare haematological diseases. Vaccinex will use its proprietary antibody discovery technologies to create fully human antibodies with the same specificity and function as OPi's panel of existing mouse monoclonal antibodies, some of which have already shown promising results in human trials. Under the agreement, Vaccinex will have the opportunity to participate as a co-development partner in certain markets.

Using its proprietary vaccinia vector technology, Vaccinex has developed unique library-based antibody discovery platforms capable of directly expressing bivalent, fully human antibodies in mammalian cells. Unlike antibody systems utilizing phage display libraries or transgenic mice, Vaccinex's technology offers the potential to directly generate fully functional antibodies against difficult targets such as homologous proteins and multi-pass membrane receptors. In addition, Vaccinex's technology can be used to fully humanize mouse and other non-human antibodies.

"We are excited about this collaboration with Vaccinex", said Gilles Alberici, CEO, President and founder of OPi. "Since OPi's inception four years ago, we have demonstrated our ability to grow in developing new compounds. Vaccinex's innovative antibody discovery technology will enable us to make a technological leap to develop new fully human antibodies aiming at treating haematological diseases."

Maurice Zauderer, President and CEO of Vaccinex commented, "We are very enthusiastic about applying our antibody discovery competencies to promote the development of new treatments for blood-based cancers and other diseases. We are pleased to be working with OPi's dedicated group of scientists, physicians and pharmacists to successfully bring product candidates into clinical development."

OPi, Pharmaceuticals for Rare Diseases

Founded in 1999, OPi is a European integrated biopharmaceutical company whose mission is to develop and market pharmaceuticals aimed at treating patients suffering from rare and severe diseases. The company has already one product approved in Europe and several products under clinical development. Innovation and medical needs are the mainstays of OPi's approach. For additional information, please visit the company's website at www.orphan-opi.com.

Vaccinex

Vaccinex is a privately held biotechnology company engaged in the discovery and development of novel therapeutic antibodies. The company is leveraging the capabilities of its proprietary antibody technology to develop its own pipeline of therapeutic antibody products, while using near-term revenues from antibody discovery collaborations to help support its operating costs. The firm is headquartered in Rochester, New York and currently has 37 employees. For additional information, please visit the company's website at www.vaccinex.com.

Contacts:

OPi
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e-mail : opi@orphan-opi.com - Web Site : www.orphan-opi.com

Vaccinex

Alliance Vaccinex

Lonza Biologics and Vaccinex Announce Strategic Alliance

07/11/2003

Lonza Biologics and Vaccinex Announce Strategic Alliance

Lonza Biologics (Lonza) and Vaccinex, Inc. today announced a strategic alliance that offers their respective clients a broad range of antibody discovery and manufacturing services.

Lonza will provide Vaccinex, its clients and co-development partners with access to its proprietary Glutamine Synthetase Gene Expression system, which offers important advantages including high yielding cell lines, ease of use and regulatory familiarity. In addition, for a period of five years, Lonza will provide dedicated access to its cGMP manufacturing facilities for the clinical production of recombinant proteins and antibody products. Vaccinex will offer antibody discovery services to Lonza's clients seeking to identify novel therapeutic antibodies. Vaccinex's library-based antibody discovery technology is unique in that it can directly express complete, fully human antibodies in mammalian cells. Both parties will assist each other in the marketing of their respective antibody service offerings to clients.

"By coordinating the discovery and clinical manufacturing processes, we are able to offer our clients a more efficient and predictable pathway for product development. In addition, Vaccinex, our clients and co-development partners will benefit from obtaining access to Lonza's world-class antibody manufacturing facilities and expertise," said Dr. Maurice Zauderer, President and CEO of Vaccinex.

"Integrating Vaccinex's innovative library-based antibody discovery technology with the GS Gene Expression System will offer true value to customers by producing substantial quantities of high quality, fully functional human monoclonal antibodies that would have been difficult to identify with other systems. Moreover this relationship will facilitate a rapid and smooth transition from product discovery to clinical manufacture," said Markus Gemuend, CEO of Lonza Group.

About Lonza
Lonza is a Life Sciences driven company headquartered in Switzerland, with sales of CHF 2.54 billion in 2002 and operating 18 production and R&D facilities in 8 countries. It employs 6 200 people worldwide and is the leading custom manufacturer of active chemical ingredients, intermediates and biotechnology solutions to the pharmaceutical and agrochemical industries. It also offers organic intermediates for a wide range of applications and provides antimicrobial and associated products as well as polymer intermediates and compounds. For more information on Lonza please visit the company's website at www.lonza.com.

About Vaccinex, Inc.
Vaccinex is a privately held biotechnology company engaged in the discovery and development of novel therapeutic antibodies. Therapeutic antibodies have become one of the largest and fastest growing sectors of biotechnology, currently representing approximately 20% of all drugs in the biotechnology pipeline. Vaccinex's antibody discovery platform is one of the only library-based antibody technologies that can directly express complete, fully human antibodies in mammalian cells. The company is commercializing this technology by offering antibody discovery services to clients worldwide and is developing its own proprietary therapeutic products, initially focused on cancer. The firm is headquartered in Rochester, New York and currently has over 30 employees. For additional information, please visit the company's website at www.vaccinex.com.

For further information please contact:

Biocon ties up with Vaccinex to co-develop antibody drugs

The Business Standard: November 19, 2004

Bangalore: Biocon Limited, the Bangalore-based biotechnology company and Vaccinex Inc. have announced a broad strategic partnership to discover and co-develop at least four therapeutic anti-body products.

Vaccinex is a New York-based privately held biotechnology company engaged in the discovery and development of novel therapeutic antibodies. Biocon and Vaccinex will jointly work to identify promising antibody candidates and move them rapidly into clinical development.

Both companies plan to focus on antibody products directed at cancer, inflammation and auto-immune diseases. As part of the collaboration, Biocon will also make an equity investment in Vaccinex.

"Vaccinex has a strong discovery-led platform that will be beneficial to Biocon and the two companies will work jointly," Kiran Mazumdar-Shaw, chairman and managing director, Biocon Limited, said.

The collaboration combines Vaccinex's capabilities to discover fully human monoclonal antibodies using its proprietary anti-body discovery technology and Biocon's expertise in clinical research and biologics manufacturing.

According to Maurice Zauderer, president and CEO of Vaccinex, "By combining our respective skills and knowledge, this collaboration will allow Biocon and Vaccinex to accelerate introduction of , high value therapeutic antibody products in India and the West."

Vaccinex has also accepted the nomination of Dr Bala Manian, the eminent California scientist and entrepreneur as Biocon's nominee director to the Vaccinex board of directors. This will take effect once regulatory procedures are completed.

Vaccinex, with the help of its proprietary vaccinia vector technology, has developed the only library-based antibody discovery platform capable of directly expressing bivalent, fully huma antibodies in mammalian cells.

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